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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,067	SUTTER ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-14,16-18,20-22 and 25-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-14,16-18,20-22 and 25-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Art Examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Stacy Chen in Art Unit 1648.

Response to Amendment

2. The following rejections are withdrawn:

- The rejection of claims 14 and 15 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn with respect to claim 14 in view of cancelled claim 15.
- The rejection of claim 10 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn in view of Applicant's persuasive arguments.
- The rejection of claims 11, 12, and 18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 12-19, and 23-31 of U.S. Patent No. 7,049,145 in view of the teachings of Schneider et al. and Kumar et al. as applied above, is withdrawn upon further consideration of the claimed subject matter in both the patent and the instant application.
- The provisional rejection of claims 1, 2 and 6-25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5, 7, 11, and

12 of copending Application No. 11/375,159, now US Patent 7,767,209, in view of in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above, is withdrawn upon further consideration of the claimed subject matter in both the patent and the instant application. The Office notes that there were two rejections over the same copending Application. Both rejections are withdrawn.

Specification

3. The specification remains objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: Applicant is requested to insert antecedent basis support (acknowledging that written description support is present) for the claim limitation regarding vaccines which "do not comprise an adjuvant."

Applicant's arguments have been carefully considered but fail to persuade. The Office is not asserting that Applicant did not contemplate the embodiment of a vaccine without an adjuvant. This is not an issue of lack of written description. The Office is simply requiring that Applicant state such in the specification to provide antecedent basis support for the particular claim language.

Claims Summary

4. Claims 1, 2, 6-14, 16-18, 20-22, 25 and new claims 26-29 are pending and under consideration in the application. The claims are drawn to a recombinant MVA virus comprising

at least one nucleic acid sequence coding for at least one of following *Plasmodium falciparum* merozoite surface protein-1 (MSP-1) fragments: p42; p42 and p38; and, p42, p38, p30 and p83. The MSP-1 protein/fragments are from isolate 3D7 or FCB-1. The nucleic acid sequence encoding the MSP-1 fragments is reduced in its AT content compared to the wild-type sequence.

Specifically, the nucleic acid sequence is under the control of a promoter. The 5' end of the nucleic acid sequence is fused with a coding sequence for a signal peptide sequence, which controls the secretion and/or localization of the MSP-1 fragment. In another embodiment, the signal peptide sequence controls the glycosylphosphatidylinositol anchoring of the MSP-1 fragment.

Also claimed is a vaccine and vaccine kit comprising the recombinant virus and a pharmacologically compatible carrier. In one embodiment, the vaccine does not comprise an adjuvant. In another embodiment, the vaccine further comprises a recombinant MSP-1 protein. The vaccine and vaccine -kit further comprise an additional component that is suitable for simultaneous, sequential or separate administration along with the recombinant virus. The additional component is MSP-1 (understood to be an intact protein), a fragment of MSP-1, a nucleic acid sequence coding for MSP-1, or a nucleic acid sequence coding for a fragment of MSP-1.

Also claimed is a method of producing the recombinant MVA, by transfecting a eukaryotic host cell with a transfer vector comprising the nucleic acid sequence described above, and may further comprise a selection marker. The nucleic acid sequence is flanked by MVA sequences 5' and/or 3', suitable for homologous recombinant. The transfected cells are infected

an MVA virus, cultivated and isolated (*e.g.*, from the culture supernatant or from the cultivated host cells).

Also claimed is a method for the therapy of malaria, comprising administering the recombinant MVA described above, and MSP-1 (intact or fragment), or a nucleic acid sequence encoding MSP-1 (intact or fragment). The MSP-1 fragments are selected from p42, p38, p30, p83, , p33, p19, and a combination thereof.

Claim Objections

5. Claims 22 and 27 are objected to for minor informalities. Claim 22 has back-to-back commas in section a). Claim 27 lacks a period at the end of the sentence. Correction is required.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 6-14, 16-18, 20-22 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the teachings of Schneider *et al.* (*Nature Medicine*, 1998, Vol. 4, No. 4, pages 397-402) in view of Yang *et al.* (*Vaccine*, 1997, Vol. 15, No. 12/13, pages 1303-1313), Kumar *et al.* (*Immunology Letters*, April 2002, Vol. 81, pages 13-24) and Bujard *et al.* (WO 98/14583, 1998). It is noted that claim 26 was not included in the statement of the rejection in the Office action of 3/1/10. However, it is clear that claim 26 was indeed intended to be included in the

rejection, evidenced by the reference to claim 26 on pages 8-9 (bridging paragraph) of the Office action. The present rejection is extended to new claims 27-29, drawn to a vaccine kit whose components are identical to those of the vaccine claims. Claim 29 is drawn to an embodiment wherein the components are suitable for simultaneous, sequential or separate administration. This limitation has been addressed in the obviousness rejection in the Office action of 3/1/10, page 8, first full paragraph, for example, which discusses a priming/boosting technique.

It is noted that the statement of the rejection, particularly on page 12 of the prior action, indicated that the teachings of the prior art would have rendered obvious the production of a DNA vaccine, and particularly a plasmid DNA vaccine, expressing the *P. falciparum* p42 antigen.

As was previously described, the present claims are drawn to recombinant modified vaccinia virus Ankara vectors encoding the p42 fragment of MSP-1, particularly from the isolate 3D7, and to methods for the production of the vector, and the use of the vector as a vaccine against malaria. The teachings of the prior art would have rendered obvious the production of a DNA vaccine, and particularly a plasmid DNA vaccine, expressing the *P. falciparum* p42 antigen. The teachings of the prior art also render obvious the construction of MVA vectors encoding the p42 fragment (and the other fragments identified in the cited art) as a booster vaccine for the plasmid DNA vaccines.

This is because, each of the Kumar and Schneider references teach the use of vaccinia virus vectors as effective boosters for prior primary administrations of other anti-malarial vaccines. While, as noted by the Applicant, Schneider indicates that MVA may or may not be an effective primary composition, the teachings in the art provide those of ordinary skill in the art

with a reasonable expectation of success in the use of the MVA as a booster vaccine. Thus, while the teachings of Schneider provide evidence that it may not have been obvious (on the basis of unpredictability) to use the claimed MVA vectors in a primary vaccination, the teachings of the art indicate that the converse is true with respect to its use as a booster composition.

Applicant's assertion that Kumar only teaches the administration of the MVA to cells for CTL analysis is noted. Nonetheless, the reference does teach the use of viral vectors for the purpose of boosting a primary administration of a DNA vaccine, see page 14 (right column, 2nd full paragraph) and page 23, top paragraph (which indicates that a DNA plasmid vaccine could be included as part of a multi-antigen DNA vaccine). This argument by the Applicant is therefore not found persuasive. With regard to the Zavala reference (2001, *Virology*, 280:155-159), it is noted that only one page of the reference was provided to Applicant in the Office action of 3/1/10. The Office will not be referring to the Zavala reference since the reference is not required for the rejection, but was merely used a supplemental reference. Applicant's remarks concerning the Zavala reference are moot.

From the teachings of these references, it would have been obvious to those of ordinary skill in the art to use p42 antigen identified as a protective antigen in Kumar as the encoded antigen in the plasmid DNA priming/MVA boosting technique suggested by the teachings of Kumar and Schneider.

The additional arguments presented in the Response each assert deficiencies in the individual applied references. It is established in the patent law that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See e.g., *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981);

In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). These remaining arguments are therefore not found persuasive.

It is noted that the teachings of Bujard are applied primarily to render obvious the claim limitations requiring the reduced adenine and thymine content of the MSP-1 fragment coding sequences, now found only in claims 25 and 26. As the reference teaches the application of such a method to the production of *Plasmodium* vaccines, such as live vaccinia virus based vaccines (see e.g., column 8, of U.S. 6,933,130- the U.S. national stage of the Bujard reference), it would have been obvious to those of ordinary skill in the art to apply the stabilization method of that reference to the p42 coding sequences in the plasmids and MVA vectors suggested by Schneider and Kumar.

Similarly, the teachings of Yang primarily render obvious the inclusion of the signal sequences referred to in claims 6-10. In particular, the reference teaches that the inclusion of such signal sequences in vaccinia vectors encoding the MSP-1 antigens of the reference resulted in the surface expression of the antigens on the infected cells, which resulted in an enhanced response against the antigens. Thus, it would have been obvious to those of ordinary skill in the art to have used this technique to enhance the immunogenicity of the antigens encoded by the MVA vectors of Schneider. This is particularly the case when the teachings of Langford *et al.* (*Molec Cell Biol* 6:3191-99- cited on page 1311 of Yang) are considered. This reference indicates that the surface expression through the inclusion of signal sequences in antigens expression by live virus vectors generally results in increased immunogenicity. Thus, those of ordinary skill in the art would have had a reasonable expectation of success in the application of this immunogenicity enhancing method to the vectors suggested by Schneider and Kumar.

In addition to the teachings previously described, it is also noted that the vaccinia vector described by Kumar includes a selection marker, and that this selection marker was accepted in the art as also useful in the vaccinia MVA vector. See e.g., Staib *et al.*, *Biotechniques* 28:1137. Thus, it would have been obvious to those of ordinary skill in the art to have used this selection marker in the vaccinia MVA vector of Schneider as a means for selecting MVA properly incorporating the MSP-1 coding sequence.

For the reasons above and of record, Applicant's arguments are not found persuasive, and the rejection is maintained.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 6-14, 16-18, 20-22 and 25-29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8, 12-19, and 23-31 of

U.S. Patent No. 7,198,934, or of claims 1-5, 8-11, 16-19, 24-28, 31, and 33 of US Patent 6,440,422; in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. The patented claims are generic to the present claims, and fail to specify the use of the MSP-1 fragments, the signal sequences, and the inclusion or co-administration of the additional antigenic agents. However, such limitations would have been obvious based on the teachings of the secondary references as described above and previously. The present claims therefore represent an obvious embodiment of the patented claims

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the Office has not provided a rationale as to why any of the instant claims would be considered an obvious variation over the claims of the patents. In response to Applicant's arguments, the rationale is provided in the obviousness rejection set forth above. Given the generic structure of the patented claims, it would have been obvious to modify that generic structure in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above.

8. Claim 17 remains provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 and 21-24 of copending Application No. 12/523,023 in view of in view of the teachings of Schneider et al., Yang et al., Kumar et al., Bujard et al., and Sedegah et al. as applied above. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims read on a method of using the products of the copending application, wherein at least the use of the products as vaccines are taught by the copending specification and claims. The additional

limitations of the present claims would have been obvious in view of the teachings of the secondary references as described above.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

This rejection is necessitated by the decision of the Court of Appeals for the Federal Circuit in Pfizer Inc. v Teva pharmaceuticals USA Inc., 86 USPQ2d 1001, at page 1008 (March 2008), which indicates that there is no patentable distinction between claims to a product and a method of using that product disclosed in the specification of the application and that the preclusion of such a double patenting rejection under 35 USC 121 does not apply where the present application is other than a divisional application of the patent application containing such patentably indistinct claims.

Conclusion

9. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30), alternate Fridays off,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648